

## WHAT IS CLAIMED IS:

1. A pharmaceutical composition for pulmonary delivery of an oligonucleotide comprising at least one oligonucleotide wherein the sugar moiety of at least one nucleoside unit of said oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage within said oligonucleotide is not a phosphodiester or a phosphorothioate linkage.

2. The pharmaceutical composition of claim 1, wherein the sugar moiety of at least one nucleoside unit of said oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety.

3. The pharmaceutical composition of claim 2 wherein said nucleoside unit is a 2'-O-substituted nucleoside unit.

4. The pharmaceutical composition of claim 3 wherein said 2'-O-substituent of said 2'-O-substituted nucleoside unit is a 2'-O-alkoxyalkoxy substituent.

5. The pharmaceutical composition of claim 3 wherein said 2'-O-substituent of said 2'-O-substituted nucleoside unit is a 2'-O-dialkylaminooxyalkyl substituent.

6. The pharmaceutical composition of claim 1, wherein at least one internucleotide linkage within said oligonucleotide is not a phosphodiester or a phosphorothioate linkage.

7. The pharmaceutical composition of claim 6 wherein at least one internucleotide linkage within said oligonucleotide is a 3'-methylenephosphonate, a non-phosphorus containing oligonucleoside linkage, a 2'-5' linkage or is a 3'-deoxy-3'-amino phosphoramidate linkage.

8. The pharmaceutical composition of claim 1 further comprising one or more pharmaceutically acceptable carriers.

5 9. The pharmaceutical composition of claim 1 wherein said composition is in aqueous media.

10. The pharmaceutical composition of claim 9 wherein said aqueous media is sterilized, pyrogen free water.

10 11. The pharmaceutical composition of claim 9 wherein said aqueous media is saline solution.

12. The pharmaceutical composition of claim 1 wherein said composition is a powder.

15 13. The pharmaceutical composition of claim 1, wherein said oligonucleotide is an antisense oligonucleotide.

14. The pharmaceutical composition of claim 13 wherein said antisense compound modulates the expression of a protein or modulates a rate of cellular proliferation.

20 15. The pharmaceutical composition of claim 14 wherein said antisense oligonucleotide modulates expression of a cellular adhesion protein.

16. The pharmaceutical composition of claim 13, wherein the antisense oligonucleotide is antisense to a genetic sequence implicated in a disease or disorder.

25 17. The pharmaceutical composition of claim 13, wherein said disease or disorder is asthma, a cancer of the lung, pulmonary fibrosis, rhinovirus, tuberculosis, bronchitis, or pneumonia.

18. The pharmaceutical composition of claim 13, wherein said antisense oligonucleotide is antisense to a portion of a gene coding for a cytokine.

5 19. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for ICAM-1, ELAM-1, VCAM-1, B7-1, B7-2, CD40, LFA-3, PECAM-1, a ras oncogene, an H-ras oncogene, a K-ras oncogene, or Protein Kinase C.

10 20. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a unique portion of the genome of *Mycobacterium tuberculosis*, *M. bovis*, or *Streptococcus pneumoniae*.

15 21. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for ICAM-1.

22. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for ELAM-1.

20 23. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for VCAM-1.

24. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for B7-1.

25 25. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for B7-2.

26. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a

portion of a gene coding for CD40.

27. The pharmaceutical composition of claim 1 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for LFA-3.

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28. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for PECAM-1.

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29. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for a ras oncogene.

30. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for H-ras oncogene.

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31. The pharmaceutical composition of claim 13 wherein said antisense oligonucleotide is antisense to a portion of a gene coding for K-ras oncogene.

32. The pharmaceutical composition of claim 13, wherein said antisense oligonucleotide is antisense to a portion of a gene coding for Protein Kinase C.

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33. The pharmaceutical composition of claim 13 comprising more than one antisense oligonucleotide.

34. The pharmaceutical composition of claim 1 wherein said oligonucleotide is a ribozyme, an external guide sequence, or an antisense peptide nucleic acid.

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35. The pharmaceutical composition of claim 1 wherein said oligonucleotide is an aptamer or a molecular decoy.

36. The pharmaceutical composition of claim 9

wherein said aqueous media is sterilized, pyrogen free buffer solution.

37. A method for the administration of an nucleic acid therapeutic or diagnostic composition comprising:

preparing a nucleic acid therapeutic or diagnostic composition;  
aerosolizing the nucleic acid composition;  
introducing the aerosolized nucleic acid composition into the lung of a mammal; and

wherein the aerosolized nucleic acid composition comprises at least one oligonucleotide wherein the sugar moiety of at least one nucleoside unit of said oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety or at least one internucleotide linkage within said oligonucleotide is not a phosphodiester or a phosphorothioate linkage.

38. The method of claim 37, wherein the sugar moiety of at least one nucleoside unit of said oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety.

39. The method 38 wherein said nucleoside unit is a 2'-O-substituted nucleoside unit.

40. The method of claim 39 wherein said 2-O-substituent of said 2'-O-substituted nucleoside unit is a 2'-O-alkoxyalkoxy substituent.

41. The method of claim 39 wherein said 2-O-substituent of said 2'-O-substituted nucleoside unit is a 2'-O-dialkylaminoalkoxy substituent.

42. The method of claim 37, wherein at least one internucleotide linkage within said oligonucleotide is not a phosphodiester or a phosphorothioate linkage.

43. The method of claim 42 wherein at least one internucleotide linkage within said oligonucleotide is a 3'-methylenephosphonate, a non-phosphorus containing oligonucleoside linkage, a 2'-5' linkage or is a 3'-deoxy-3'-amino phosphoramidate linkage.

44. The method of claim 37 wherein said pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers.

45. The method of claim 37 wherein said nucleic acid therapeutic or diagnostic composition is in aqueous media.

46. The method of claim 37 wherein said nucleic acid therapeutic or diagnostic composition is sterilized, pyrogen free water.

47. The method of claim 37 wherein said nucleic acid therapeutic or diagnostic composition is saline solution.

48. The method of claim 37 wherein said nucleic acid therapeutic or diagnostic composition is a powder.

49. The method of claim 37 wherein the nucleic acid therapeutic composition contains more than one oligonucleotide.

50. The method of claim 37 wherein the oligonucleotide is an antisense oligonucleotide.

51. The method of claim 37 wherein the nucleic acid therapeutic composition is aerosolized solution consists essentially of an antisense oligonucleotide in saline solution.

52. A method of treating an animal having or

5 suspected of having a disease or disorder that is treatable  
with one or more nucleic acids comprising administering a  
therapeutically effective amount of an aerosolized nucleic  
acid composition to the lung of the animal, wherein the  
aerosolized nucleic acid composition comprises at least one  
oligonucleotide wherein the sugar moiety of at least one  
nucleoside unit of said oligonucleotide is not a 2'-  
deoxyribofuranosyl sugar moiety or at least one  
internucleotide linkage within said oligonucleotide is not  
10 a phosphodiester or a phosphorothioate linkage.

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AS  
15 53. A method of investigating the role of gene  
or gene product in an animal other than a human comprising  
administering a therapeutically effective amount of an  
aerosolized nucleic acid composition to the lung of the  
animal, wherein the aerosolized nucleic acid composition  
comprises at least one oligonucleotide wherein the sugar  
moiety of at least one nucleoside unit of said  
oligonucleotide is not a 2'-deoxyribofuranosyl sugar moiety  
or at least one internucleotide linkage within said  
20 oligonucleotide is not a phosphodiester or a  
phosphorothioate linkage.

25 54. A method for delivering an oligonucleotide  
therapeutic or diagnostic compound to the lung of an animal  
comprising applying to said lung a pharmaceutical  
composition according to claim 1.

55. The method of claim 54 wherein said  
oligonucleotide is delivered within cells of said lung.

56. The method of claim 55 wherein said animal  
is known or suspected to suffer from a disease or disorder.

30 57. The method of claim 56 wherein said disease  
or disorder is asthma, a cancer of the lung, pulmonary  
fibrosis, rhinovirus, tuberculosis, bronchitis, or  
pneumonia.

58. The method of claim 37 wherein the nucleic acid therapeutic composition is aerosolized solution consists essentially of an antisense oligonucleotide in buffer solution.

59. A method of modulating the expression of a gene in an animal comprising administering to said animal the pharmaceutical composition of claim 1.

60. A method of modulating the expression of a gene in an animal comprising administering to said animal the pharmaceutical composition of claim 1.

61. A medical device for pulmonary delivery of an aerosol comprising a pharmaceutical composition in accordance with claim 1.

62. A pharmaceutical composition according to claim 1, wherein said oligonucleotide is selected from the group consisting of ISIS-15839, ISIS-13312, ISIS-9605, ISIS-9606, ISIS-14859, ISIS-17709, ISIS-17044, ISIS-28089 and ISIS-104838.

63. A method according to claim 37, wherein said oligonucleotide is selected from the group consisting of ISIS-15839, ISIS-13312, ISIS-9605, ISIS-9606, ISIS-14859, ISIS-17709, ISIS-17044, ISIS-28089 and ISIS-104838.